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### REMARKS

Claims 1-10 and 14-16 are pending; claims 6, 10, and 14 were allowed in the Office Action mailed August 20, 2001.

### The Amendments

The amendments to the claims (i.e., the new claims) are intended merely to more appropriately and fully cover the scope of the invention as it applies specifically to testosterone as the treating agent. The amendments to Claims 1 and 7 are intended merely to further clarify that "progressive hydration" formulations are intended to protect ingredients from moisture initially, and that they differ from prior art compositions that contain significant amounts of water. There is no intent or expectation that any of these new claims narrows the scope of any claim or claim term or limitation, or presents any narrower claim, than those pending, for any patentability reason or for any other reason.

The amendments to the specification and drawings are meant merely: (a) to submit formal drawings for Figures 1 and 2, and to re-label and move Charts 1 to 4, from within the specification as filed, to formal drawings labeled Figures 3 to 6; (b) to provide better copies of Tables 1-5; and (c) to amend the specification discussing the charts and drawings to reflect these changes. None of these changes is expected or intended to have any effect on the scope or substance of the inventions herein, or specifically of any of the claims or claim terms. There is no new matter added by any of these replacement Figures, Charts, and Tables.

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254/304**Rejection of Claims Under 35 USC § 102**

Claims 1, 3-5, 7-9, 15, and 16 were rejected under 35 USC § 102 as being anticipated by Bologna U.S. Patent No. 5,543,150 ("Bologna"). Bologna is described as disclosing "a composition comprising progesterone, cross-linked polycarboxylic acid (polycarbophil), and water soluble polymer (Carbopol 934P)," and to teach "a method of delivering the composition to a mucosal surface (vaginal cavity). Progressive hydration does not mean that the composition is free of water."

Applicants respectfully disagree with the rejection. Viewed properly and in context, Bologna simply is not relevant to the instant invention -- progressive hydration formulations that protect sensitive ingredients from moisture for an extended period of time.

It is true that "progressive hydration" does not mean that the composition is completely free of water. The instant invention does not contemplate a completely water-free formulation. Nevertheless, for a formulation to progressively hydrate as contemplated by the instant invention -- with a primary purpose being the ability to protect most of a sensitive ingredient from moisture over an extended period of time, so that the ingredient is not wetted too long before it is released to the subject's body -- it must typically contain no more than a very low amount of water, and be able to absorb relatively significant amounts of water, but only in a progressive manner over an extended period of time. Much of the tablet must remain "dry" for a significant period of time, in order to protect the sensitive ingredient from moisture.

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In contrast, there is absolutely no indication -- and no real expectation -- that the formulation discussed in Bologna initially can protect a sensitive ingredient from moisture, or that it further hydrates to any significant degree upon application, let alone in the significantly gradual, progressive manner needed in order to protect moisture-sensitive components over an extended period of time.

In particular, the formulation specifically disclosed in Bologna is prepared with a large amount (and proportion) of water -- which is to be expected, because Bologna, though being capable of being used in a tablet form, typically is used as disclosed in an aqueous gel or gel-like form. See col. 6, lines 1-3, 13-16: "The drug delivery system with the drug therein may be delivered to the vagina in a variety of fashions as are known in the art, e.g., plunger, douche, and manually.... Upon use the containers are opened and the open end is inserted into the vagina, while the other end is squeezed to expel the contents of the container into the vagina." The "preferred method of delivery" uses devices described in U.S. design patent applications Ser. Nos. 07/863,879 (U.S. Patent D345,211) and 07/862,282 (allowed but abandoned). Col. 6, lines 3-6. Both of these design patent applications address elongated delivery tubes for delivering a gel or paste to the vagina.

Similarly, in the single Example set forth at col. 6, lines 44-52, the homogeneous formulation comprises about 70-75% water -- certainly too much to protect any other ingredients from moisture. In stark contrast, the example in the instant specification reflects that the contemplated final formulations are substantially water-free. See page 14, lines 14-15 ("the granulate is dried in an oven ... until moisture content is less than 2.5%") and

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page 16, lines 14-26 (reflecting that the product is prepared without the purposeful addition of any water to the ingredients, except presumably as absorbed from the air).

Thus, the instant invention necessarily requires a formulation that initially has relatively low moisture content, in order to be able to protect an active ingredient from moisture, and to "progressively hydrate" as contemplated by the invention and disclosure. In stark contrast, Bologna does not suggest or teach any particular composition that is able to accomplish this result.

As discussed at the interview, Applicants respectfully request that this rejection be reconsidered and withdrawn.

#### **Rejection of Claims Under 35 USC § 103**

Claim 2 is rejected under 35 USC § 103 as being unpatentable over Bologna, as applied to claims 1, 3-5, 7-9, 15 and 16 above.

As discussed above, and at the Examiner Interview, Bologna does not disclose or teach any progressive hydration formulation as contemplated by the instant invention and disclosure. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

#### **Conclusion**

In light of the above remarks, Applicants respectfully request entry of the amendments, and reconsideration and withdrawal of the rejections. Recognizing that claims 6, 10, and 14 were previously allowed, Applicants respectfully solicit a Notice of

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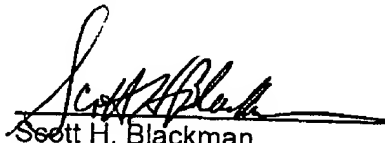
Allowance for the remaining claims 1-5, 7, 15, and 16, which had not yet been allowed, and for new claims 17-30. If it would be convenient to the Examiner, the applicants' patent attorney may be reached at the Washington, D.C. telephone number provided below.

Respectfully submitted,

LYON & LYON LLP

Dated: October 25, 2001

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## **ATTACHMENTS**

- COPIES OF FORMAL DRAWINGS, FIGURES 1-6
- COPIES OF REPLACEMENT PAGES 18-22

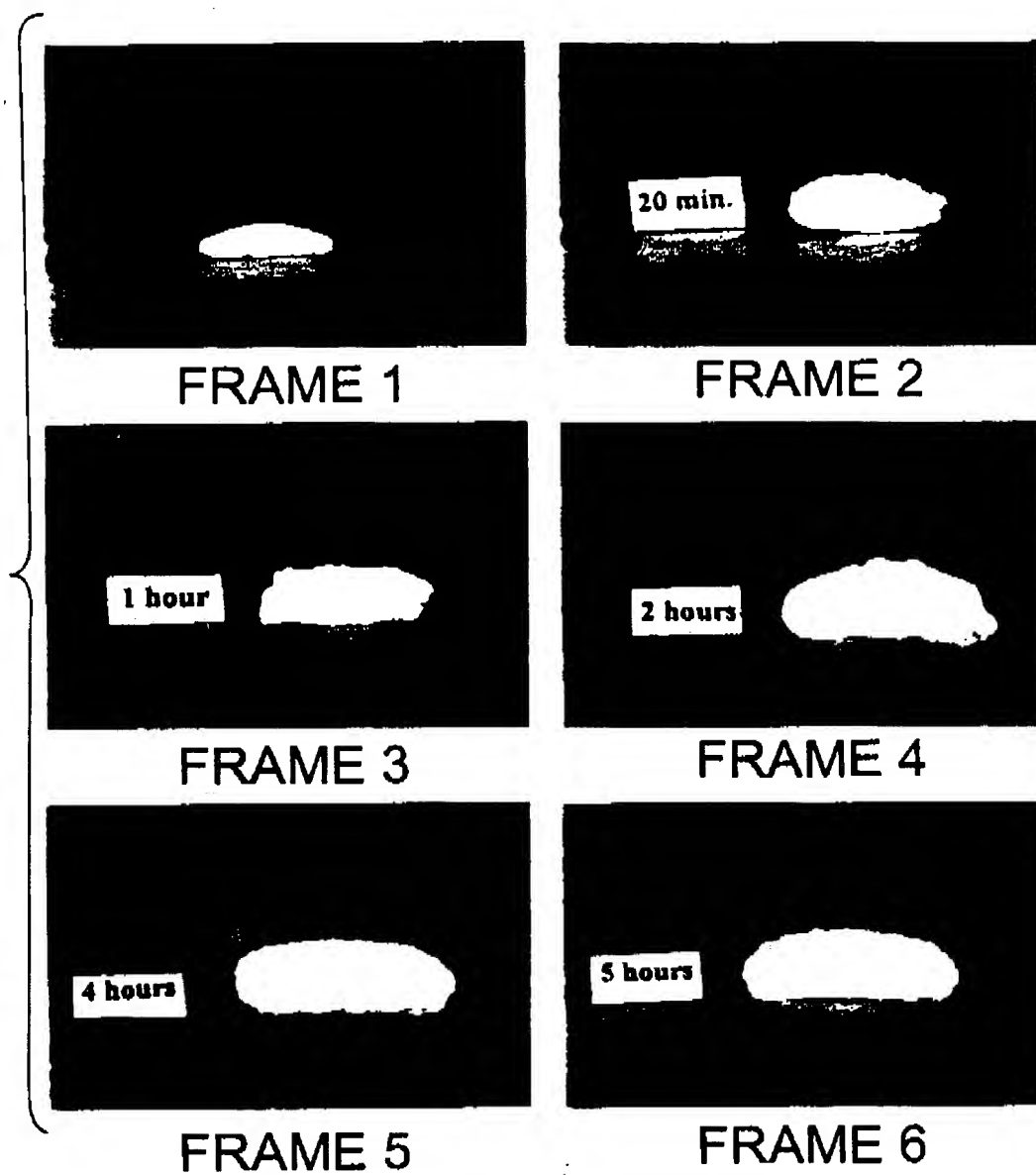


FIG. 1

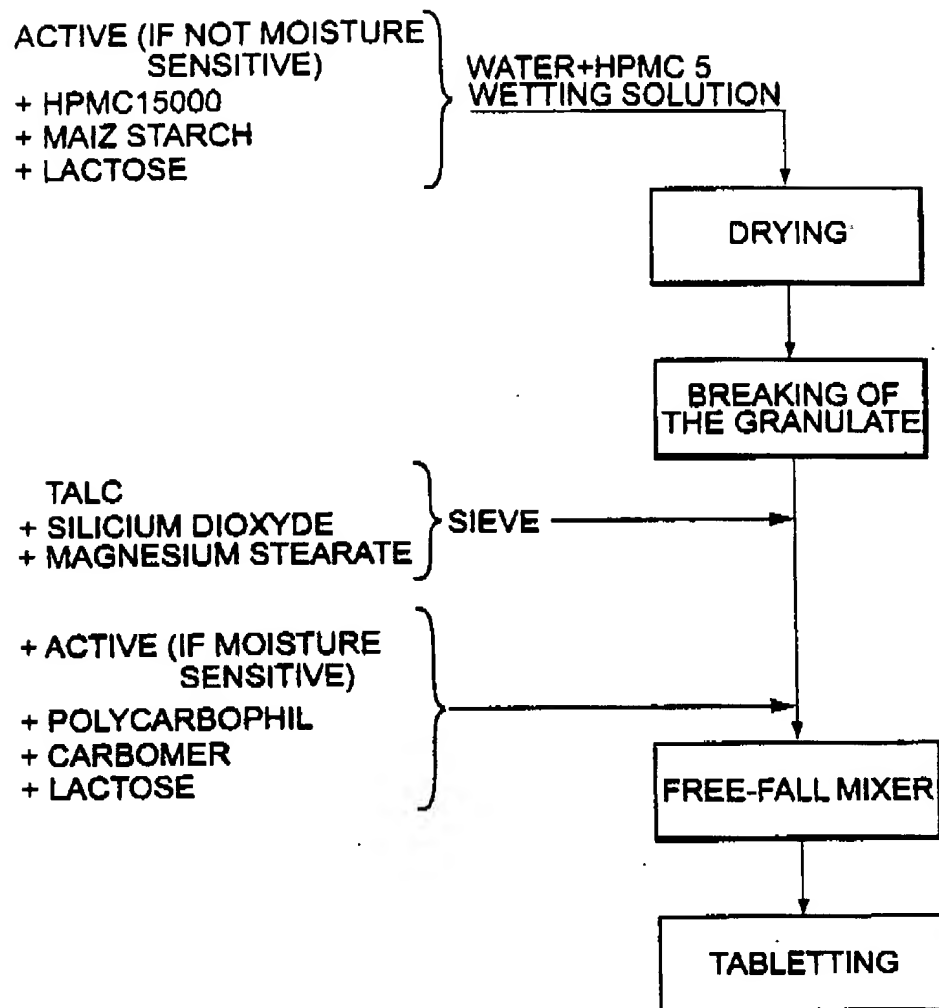


FIG. 2



## CHART 1

## FORMULA 1

% OF TESTOSTERONE RELEASE (DISSOLUTION/ROTATING PADDLE 60 RPM + PLATINUM SPIRAL)  
SINGLE VALUE ( $n=6$ ), BATCH 0069904

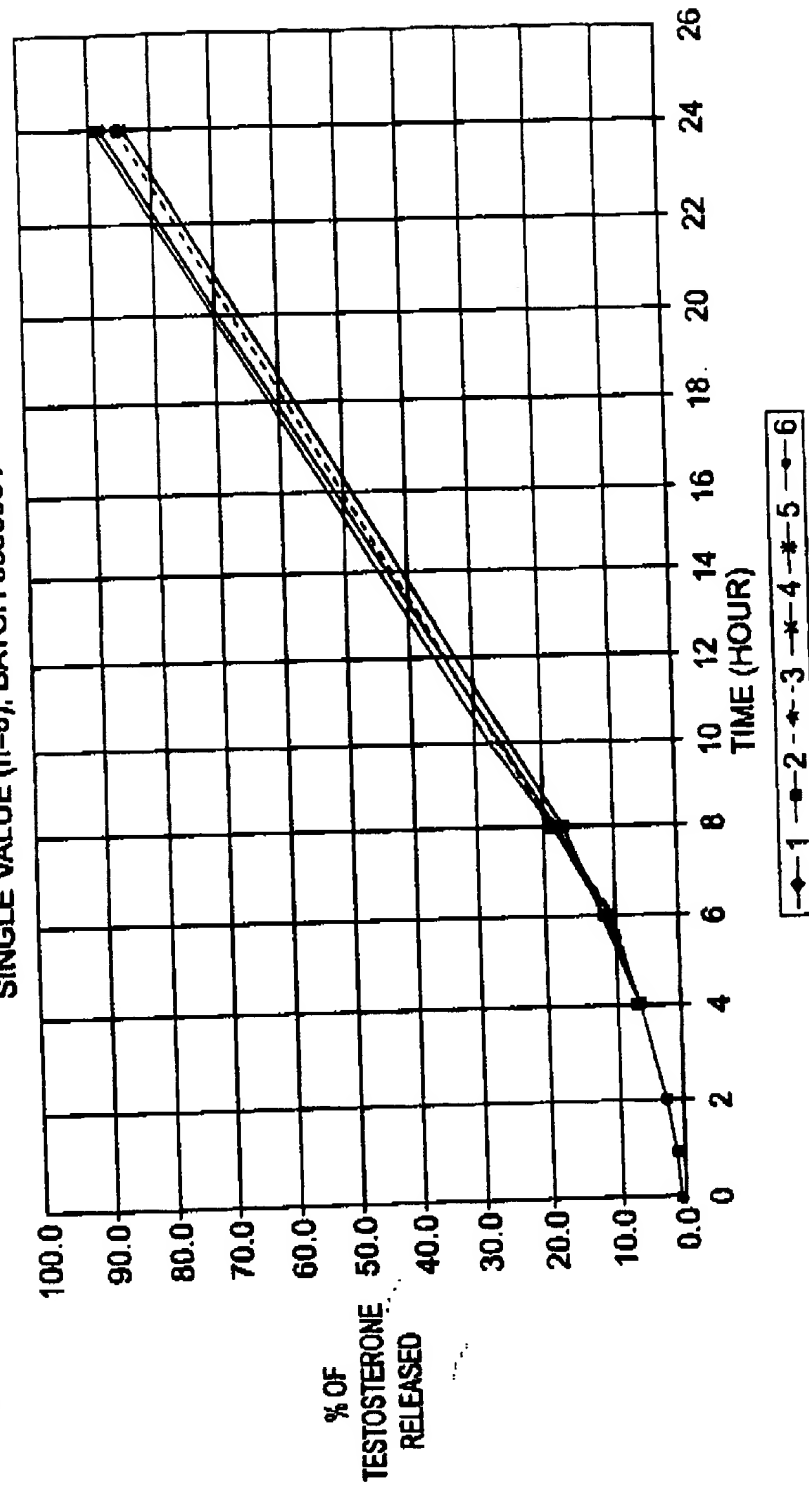


FIG. 3

CHART 2

% OF TESTOSTERONE RELEASE (DISSOLUTION/ROTATING PADDLE 60 RPM + PLATINUM SPIRAL)  
SINGLE VALUE (n=6), BATCH 0049904

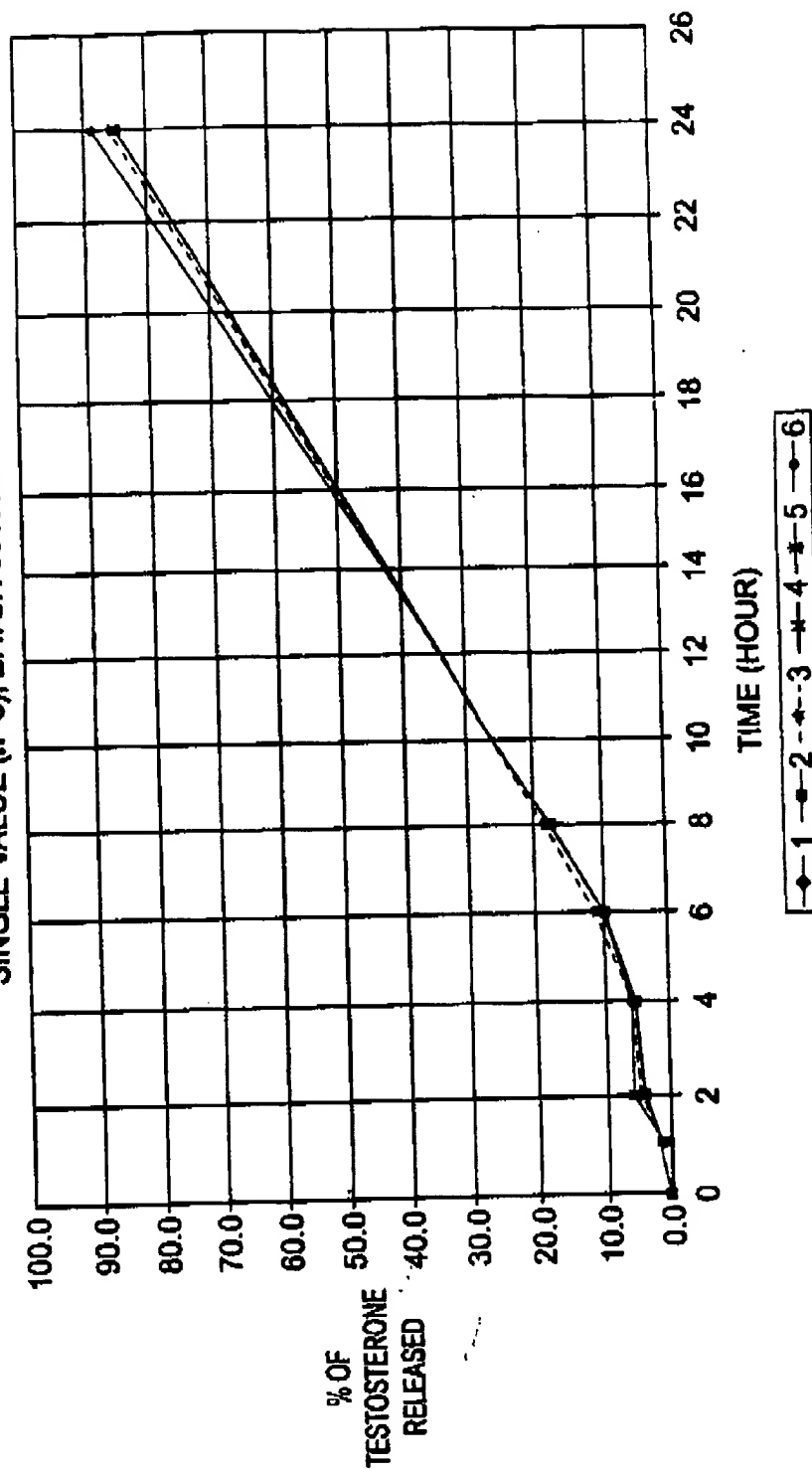


FIG. 4

# CHART 3

% OF TESTOSTERONE RELEASE (DISSOLUTION/ROTATING PADDLE 60 RPM + PLATINUM SPIRAL)  
SINGLE VALUE (n=6), BATCH 0029904

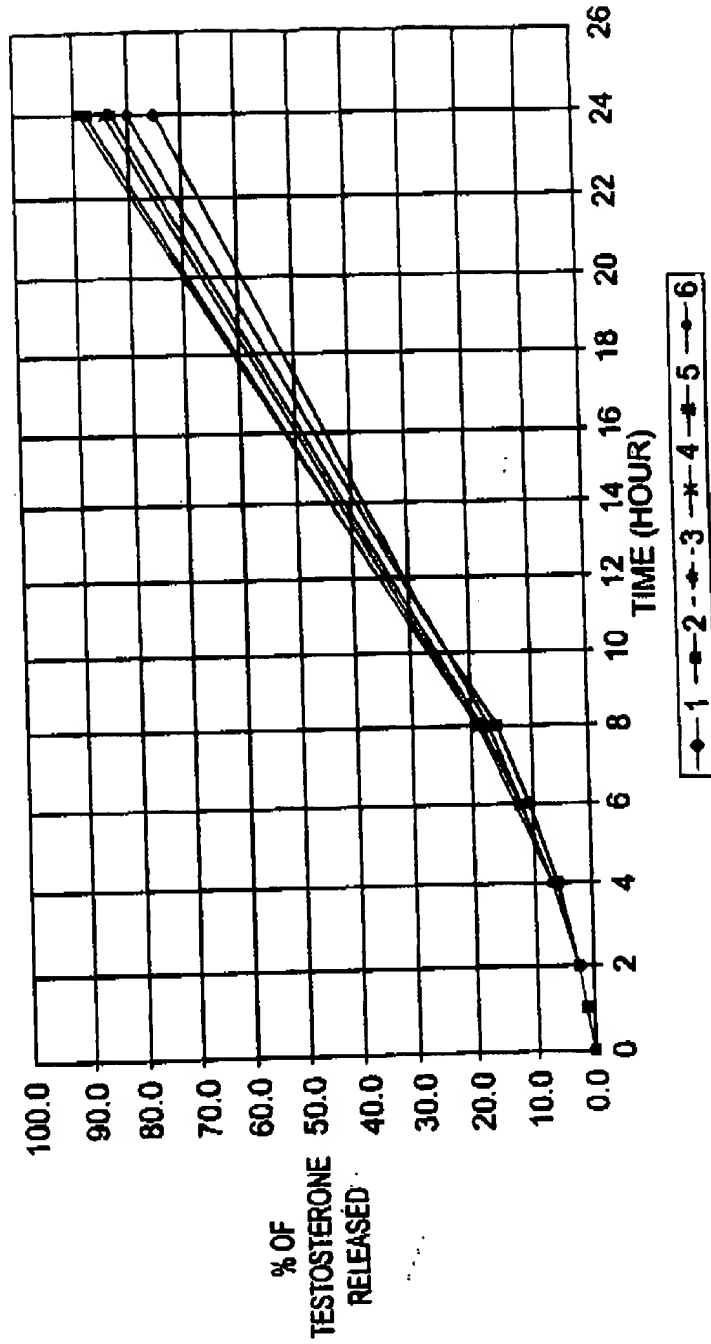


FIG. 5

CHART 4  
 % OF TESTOSTERONE RELEASE (DISSOLUTION/ROTATING PADDLE 60 RPM + PLATINUM SPIRAL)  
 SINGLE VALUE (n=6), BATCH 0019904

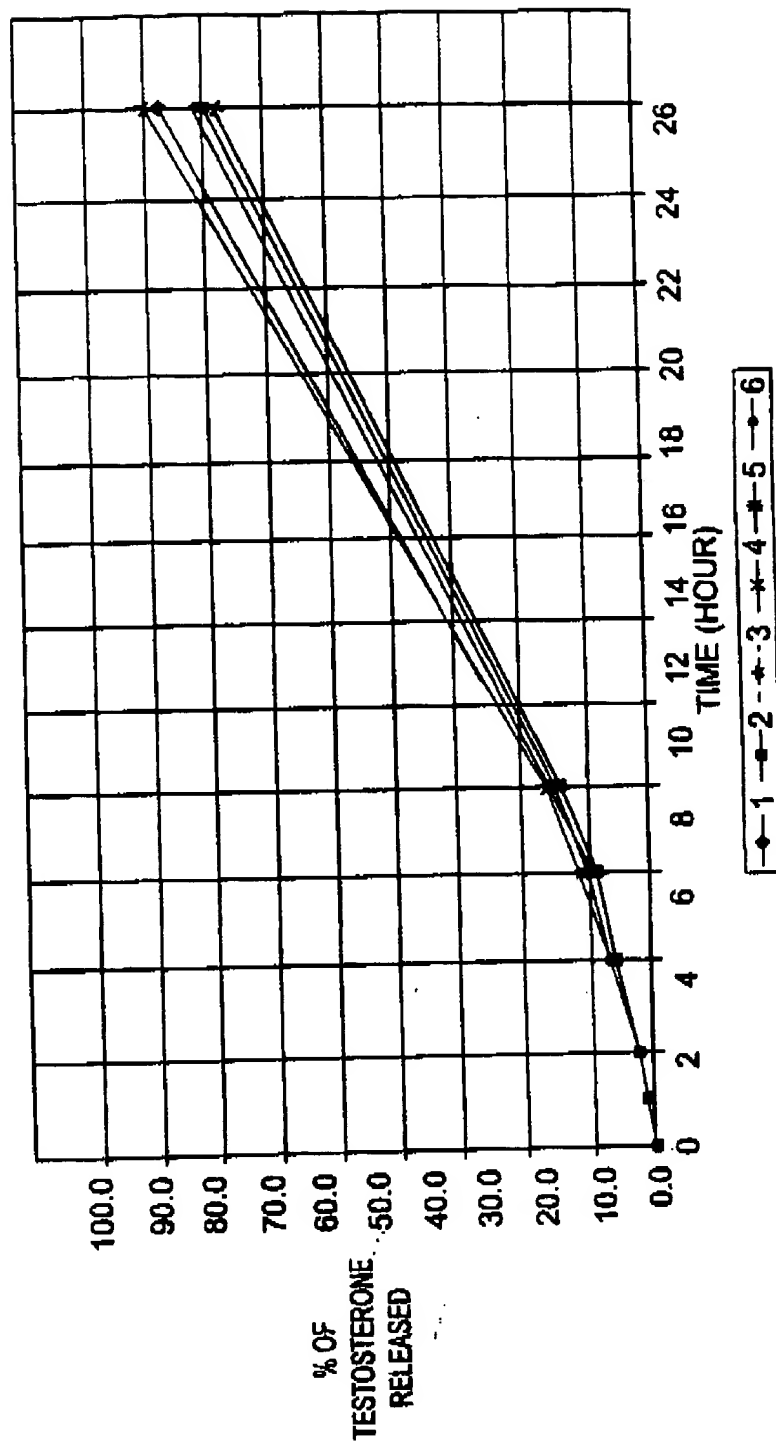


FIG. 6

## Testosterone KT

	Form 1		Form 2		Form 3		Form 4		Form 5		Form 6		Form 7		Form 8		Form 9	
	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight	mg	% by Weight
Batch #	0069904		0059904		0049904		0039904		0029904		0019904		0009904		0009904		0009904	
Testosterone	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00	30.000	24.00
HPMC-90SH-15000	31.750	25.00	30.000	24.00	28.750	23.00	27.500	22.00	26.500	21.00	26.250	21.00	26.250	21.00	26.250	21.00	26.250	21.00
Carbomer	2.500	2.00	2.500	6.00	12.500	10.00	17.500	14.00	22.500	18.00	22.500	18.00	22.500	18.00	22.500	18.00	22.500	18.00
Monohydrated Isomalt	11.375	9.10	13.875	11.10	16.375	13.10	18.875	15.10	21.375	17.10	24.500	19.60	27.625	22.10	30.825	24.10	33.750	26.60
Silica	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00	1.250	1.00
Poly-carboxylic acid (Novon AA-1)	2.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50	3.125	2.50
Carbonax 974 P	43.750	35.00	37.500	30.00	31.250	25.00	25.000	20.00	18.750	15.00	15.625	12.50	12.500	10.00	9.375	7.50	6.250	5.00
Talc	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70
Magnesium stearate	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70	0.875	0.70
Total Weight	125.000	100.00	135.000	100.00	125.000	100.00	125.000	100.00	125.000	100.00	125.000	100.00	125.000	100.00	125.000	100.00	125.000	100.00

\*Hydroxypropylmethyl cellulose

TABLE I

## TESTOSTERONE DISSOLUTION RATE -- PERCENT DISSOLUTION

BATCH: 0069904 (Formula 1)

DISSOLUTION APPARATUS: ROTATING PADDLE 60 RPM / PLATINUM WIRE SPIRAL

SAMPLE	WITHDRAW (HOUR) 0	WITHDRAW (HOUR) 1	WITHDRAW (HOUR) 2	WITHDRAW (HOUR) 4	WITHDRAW (HOUR) 6	WITHDRAW (HOUR) 8	WITHDRAW (HOUR) 24
1	0.0	0.7	1.9	7.6	10.6	16.0	83.6
2	0.0	0.6	1.7	6.7	11.7	18.0	88.5
3	0.0	0.7	2.0	6.9	11.7	17.9	84.9
4	0.0	0.6	1.7	7.0	11.2	17.1	88.3
5	0.0	0.7	1.9	6.8	10.9	17.0	87.4
6	0.0	0.7	2.1	6.6	12.4	18.3	86.6
AVERAGE VALUE	0.0	0.7	1.9	6.9	11.4	17.4	86.6

TABLE 2

## TESTOSTERONE DISSOLUTION RATE - PERCENT DISSOLUTION

BATCH: 0049904 (Formula 3)

DISSOLUTION APPARATUS: ROTATING PADDLE 60 RPM / PLATINUM WIRE SPIRAL

SAMPLE	WITHDRAW (HOUR) 0	WITHDRAW (HOUR) 1	WITHDRAW (HOUR) 2	WITHDRAW (HOUR) 4	WITHDRAW (HOUR) 6	WITHDRAW (HOUR) 8	WITHDRAW (HOUR) 24
1	0.0	0.9	3.1	5.6	10.6	16.5	83.6
2	0.0	1.1	3.1	5.6	10.5	16.9	82.2
3	0.0	1.2	3.4	6.3	11.8	18.0	83.4
4	0.0	0.9	2.9	5.4	10.8	16.7	82.7
5	0.0	1.1	4.9	5.7	10.6	16.7	83.0
6	0.0	1.0	2.9	5.6	11.0	16.8	85.6
AVERAGE VALUE	0.0	1.0	3.4	5.7	10.9	16.9	83.4

TABLE 3

## TESTOSTERONE DISSOLUTION RATE -- PERCENT DISSOLUTION

BATCH: 0029904 (Formula 5)

DISSOLUTION APPARATUS: ROTATING PADDLE 60 RPM / PLATINUM WIRE SPIRAL

SAMPLE	WITHDRAW (HOUR) 0	WITHDRAW (HOUR) 1	WITHDRAW (HOUR) 2	WITHDRAW (HOUR) 4	WITHDRAW (HOUR) 6	WITHDRAW (HOUR) 8	WITHDRAW (HOUR) 24
1	0.0	0.9	2.2	5.9	10.8	16.3	80.3
2	0.0	0.9	2.5	6.7	11.8	17.8	87.5
3	0.0	0.9	2.4	6.9	12.3	17.7	75.2
4	0.0	0.9	2.3	6.8	12.4	18.6	82.4
5	0.0	0.9	2.5	6.9	12.9	19.5	83.2
6	0.0	0.9	2.2	6.6	12.2	18.8	86.6
AVERAGE VALUE	0.0	0.9	2.4	6.6	12.1	18.1	82.5

TABLE 4



## TESTOSTERONE DISSOLUTION RATE -- PERCENT DISSOLUTION

BATCH: 0019904 (Formula 6)

DISSOLUTION APPARATUS: ROTATING PADDLE 60 RPM / PLATINUM WIRE SPIRAL

SAMPLE	WITHDRAW (HOUR) 0	WITHDRAW (HOUR) 1	WITHDRAW (HOUR) 2	WITHDRAW (HOUR) 4	WITHDRAW (HOUR) 6	WITHDRAW (HOUR) 8	WITHDRAW (HOUR) 24
1	0.0	1.2	2.1	5.9	11.1	16.1	71.7
2	0.0	0.8	2.0	5.0	9.7	14.1	70.1
3	0.0	0.9	2.3	6.4	11.3	15.8	74.6
4	0.0	0.9	2.0	5.5	10.4	15.0	68.6
5	0.0	0.8	1.8	4.9	9.9	14.6	76.6
6	0.0	0.9	1.8	4.9	9.1	13.1	70.3
AVERAGE VALUE	0.0	0.9	2.0	5.4	10.3	14.8	72.0

TABLE 5

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<b>To:</b> Examiner Alton N. Pryor Group Art Unit: 1616 U.S. Patent & Trademark Office	<b>Fax Number:</b> (703) 746-4996	<b>Phone Number:</b> (703) 308-4691
<b>From:</b> Scott H. Blackman	<b>Fax Number:</b> (202) 331-3301	<b>Phone Number:</b> (202) 974-6004
<b>Re:</b> Serial No. 09/596,073	<b>Date/Time sent:</b> 10/25/01 2:25 PM	<b>No. of Pages:</b> 26 (incl. cover)
<b>Client Name:</b>	<b>Client Matter No.:</b> 254/304	

If you do not receive all of the pages, please call Lynda A. Oertel at (202) 331-3600, extension 6003.

**Notes/Comments:**

As we discussed yesterday, please file the attached RESPONSE AND AMENDMENT.

In re Application of:	)	
William J. BOLOGNA, et al.	)	Group Art Unit: 1616
Serial No.: 09/596,073	)	
Filed: June 16, 2000	)	Examiner: Alton N. Pryor
For: BIOADHESIVE PROGRESSIVE	)	
HYDRATION TABLETS	)	

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